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(57) Abstract

The use of viscosity modifying polymer materials, commonly used as stabilisers, thickeners and emulsifiers, as tooth erosion inhibitors in acidic compositions for oral administration, especially in acidic beverages such as fruit drinks and oral healthcare products such as mouthwashes, in which the effective pH of the composition is less than or equal to 4.5.

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NOVEL COMPOSITION AND USE

The present invention relates to the use of thickening agents and stabilisers in acidic compositions for oral use such as foodstuffs and oral healthcare compositions to alleviate or inhibit the tooth damage associated with the consumption of acid, namely dental erosion.

Dental erosion describes the "pathologic, chronic, localised, painless loss of dental hard tissue chemically etched away from the tooth surface by acid and/or chelation without bacterial involvement" (Imfeld, 1996). The acids causing the erosion are derived from dietary, occupational or intrinsic sources and are not products of the intraoral flora. With the trend towards an increase in eating and drinking frequency amongst all age groups it is likely that the incidence of dental erosion will increase.

International Patent Publication (WO 97/30601) describes acid-based liquid compositions having reduced tooth erosion properties in which calcium is present in the range of 0.3 to 0.8 mol per mol of acid and which have a pH in the range 3.5 to 4.5.

Complex polysaccharide gums and other natural or synthetic polymers having viscosity modulating properties are routinely added to beverages, other foodstuffs and oral products as thickeners, stabilisers, emulsifiers and texturisers. These polymers include natural and semi-synthetic polymer materials such as alginates, locust bean gum, gellan gum, guar gum, gum arabic, xanthan gums, pectins, cellulose, and derivatives thereof; synthetic polymers such as polyvinylpyrrolidone (PVP) and other such materials known in the art.

Van der Reijden et al (Caries Res., 1997, 31, 216-23) describes a range of *in vitro* experiments with saliva substitute compositions containing thickening agents to investigate their caries-protective properties, including the effect on demineralisation and remineralisation of enamel *in vitro*. The effect of a range of polymer materials on dissolution of hydroxyapatite crystals in 50mM acetic acid at pH 5.0, and a pH cycling experiment in which bovine enamel is exposed to

demineralisation buffer (pH 4.8) and to remineralisation buffer (pH 7.0) containing a range of dissolved polymers, are described.

It has now been found that the addition of natural and synthetic polymer materials having stabilising, emulsifying and/or thickening properties to acidic foodstuffs and oral healthcare compositions reduces tooth erosion due to the loss of calcium and phosphate from tooth enamel generally associated with such products.

Furthermore, it has surprisingly been found that addition of one or more such polymer materials and calcium to an acidic composition for oral use reduces the loss of calcium and phosphate from tooth enamel to a greater extent than is conferred by addition of either polymer or calcium alone. Acidic compositions for oral use which are palatable, storage stable and effective in reducing dental erosion due to acid may accordingly be formulated with less calcium per mole of acid and at lower pH values than are disclosed in WO 97/30601

Accordingly, the present invention provides the use of a viscosity modulating polymer material as a tooth erosion inhibitor in an acidic composition for oral administration wherein the effective pH of the composition is less than or equal to 4.5.

In a further aspect the invention provides a composition for oral use comprising an acidulant, a viscosity modulating polymer material and a calcium compound wherein calcium is present in the composition in an amount up to 0.8 mol per mol of acid and the effective pH of the composition is less than or equal to 4.5.

The effective pH of compositions for oral use according to the invention will vary according to type of product, acid content and desired organoleptic properties. Suitably compositions for use in the invention will have an effective pH in the range 2.0 to 4.5, more suitably from 2.5 to 4.5, and preferably in the range 2.5 to 4.0, especially for beverages containing fruit acids.

Suitable viscosity modulating polymer materials for use in compositions of the

invention include food grade complex polysaccharide stabilisers and thickening agents such as alginates, locust bean gum, gellan gum, guar gum, gum arabic, tragacanth, carrageenan, acacia gum, xanthan gums, pectins, cellulose derivatives and other such natural or semi-synthetic polymer materials used in the field of foodstuffs and other compositions for oral use, including mixtures of one or more thereof. A suitable synthetic, non-polysaccharide viscosity modulating polymer is polyvinylpyrrolidone (PVP).

Preferred complex polysaccharide materials for use in the invention include alginates, xanthans and pectins, in particular high methoxy pectins, low ester pectins and amidated or partly amididated pectins. Suitable alginates include commercially available low, medium and high viscosity alginate products. For example, low viscosity propylene glycol alginate and sodium alginate sold under the trade names Kelcoloid LVF and Manucol LF by Monsanto; medium viscosity sodium alginate sold under the trade name Manucol DH by Monsanto; and high viscosity propylene glycol alginate sold under the trade name Kelcoloid HVF by Monsanto. Suitable xanthans include a range of products available from Monsanto under the trade names Keltrol T, Keltrol RD, Keltrol TF, Keltrol SF and Keltrol BT. Suitable pectins include high methoxy pectins such as Unipectin QC40 available from SKW Biosystems; low ester pectins such as products sold under the trade names GENU LM 22 CG and GENU LM 12 CG, partly amidated low ester pectins such as products sold under the trade names GENU LM 101 AS and GENU LM 102 AS, and amidated low ester pectins such as the product sold under the trade name GENU LM 104 AS FS, all of which pectin products are available from Hercules Ltd.

It has been shown that inhibition of dental erosion increases with increasing concentration of a given polymer material. However, viscosity is not the primary factor influencing anti-erosive potential; experiments comparing the effect of different types of polymer materials at the same viscosity have shown that they inhibit dental erosion to different extents, especially at low viscosities typical of beverage formulations. Polymer materials for use in the invention may therefore be selected and used at concentrations which may be calculated to confer a viscosity

commensurate with the required product type, ranging from liquid products such as acidic drinks through to semi-solid and solid acidic products. For example, a typical low viscosity product such as a beverage composition may incorporate a suitable polymer material at a concentration calculated to confer a viscosity below about 10cP, preferably below about 6cP. It will be appreciated that viscosity values are not absolute but are dependent on the conditions under which they are measured. Where exact values are relied on herein, the equipment used and the conditions under which it is operated are quoted.

The invention is accordingly applicable to all acidic products for oral consumption or use. These include acidic beverages, vinegars, sauces, pickles, preserves, confectionery and diverse acidic products such as acidic dairy products, and also to other substances, suitably in liquid or semi-solid form, to be taken orally such as acidic oral healthcare products, for example mouth washes, and medicines.

The invention may be applied to a variety of solid, semi-solid or liquid foodstuffs, particularly acidic beverages. These include still and carbonated alcoholic and non-alcoholic beverages, for example fruit drinks, and in particular health drinks such as blackcurrant juice drinks or vitamin added beverages. The invention also extends to concentrates and powdered forms for preparing acidic beverages. In a preferred embodiment, the acid composition is a ready to drink beverage or a drink concentrate for dilution prepared from a natural fruit juice such as blackcurrant juice.

The invention is advantageously applied to acidic compositions, in particular foodstuffs and especially beverages, containing natural and/or added acidulants. The acid composition may contain organic and/or inorganic acids and may be supplemented with vitamins such as ascorbic acid. Preferred acidulants include potable acids such as citric, malic, lactic, phosphoric, acetic and tartaric acids and mixtures thereof.

The acidulant concentration in a composition according to the invention will be determined by the type of product, the desired effective pH, the desired

organoleptic properties and the acidity of the chosen acid source. The acidity of a composition may be expressed in terms of titratable acidity which is a measure of the percentage weight of acid present in a solution as calculated from the volume of sodium hydroxide required to neutralise the acidic species present. In practice, titratable acidity is measured potentiometrically with standardised sodium hydroxide solution of a known concentration at a temperature of 20 degrees Centigrade. A typical beverage will have a titratable acidity in the range 0.01 to 4%w/w and a typical fruit-based ready to drink beverage will have a titratable acidity in the range 0.1 to 2%w/w. Typically the acid concentration in compositions of the invention, for example the acid concentration in a fruit-based product would be in the range 0.01% w/w to 4% w/w, suitably in the range 0.1% w/w to 2.5% w/w. A typical ready to drink fruit beverage based on citric and/or malic acid as the acidulant will have an acid concentration in the range 0.01 to 1.0 %w/w of the beverage composition. In a concentrate for dilution, typical citric/malic acid concentration will be in the range 0.1 to 4%w/w of the composition. Mixtures of potable acids may be used, for example mixtures of acids selected from citric, malic, phosphoric and lactic acids and other suitable food grade excipients known in the art

Foodstuffs such as beverages may be unsweetened or sweetened with natural sugars or synthetic sweeteners such as saccharine, aspartyl phenyl alanyl methyl ester, or other sweeteners known in the art. Compositions may also contain other conventional additives such as sodium benzoate, sorbic acid, sodium metabisulfite, ascorbic acid, flavourings, colourings and carbon dioxide.

The term effective pH is used in the context of the present invention to mean the pH of the composition when in liquid form or the pH of the composition before solidification (where the composition is a solid or semi-solid prepared via a liquid phase intermediate) or the pH of a solid or semi-solid composition when reconstituted or dissolved in a liquid, eg. water. The term solidification encompasses the treatment or supplementation of liquid phase intermediates to form a solid or semi-solid.

A further advantage arises from the use of low levels of calcium, suitably in the

form of an alkaline salt. When calcium is present, the buffering capacity of the formulation is reduced by partial neutralisation of the acid, which allows saliva to neutralise remaining acid residues in the mouth more rapidly.

When calcium is present, the absolute concentration is not critical as this will vary according to the nature and concentration of the acids present. Calcium may be added in any suitable form, conveniently as a soluble salt such as calcium carbonate, calcium hydroxide, calcium citrate, calcium malate, calcium citrate malate, calcium lactate, calcium chloride, calcium phosphate, calcium glycerophosphate or calcium formate or any other salt which minimises any adverse flavour contribution to the composition. Calcium content is suitably calculated on a molar basis relative to the molarity of the acidulant. Calcium may be present in an amount up to 0.8 mol per mol of acidulant. The molar ratio of calcium to acid may be from 0.01 to 0.75, is likely to be from 0.05 to 0.6, and typically from 0.1 to 0.5 for a fruit-based beverage product.

In a further aspect, the present invention provides a method of reducing the tooth erosion potential of an acidic composition for oral use comprising adding a viscosity modulating polymer material, and optionally calcium in the range 0 to 0.8 mol per mol of acid, to an acidic oral composition and, if necessary or desired, controlling the effective pH so that it is less than or equal to 4.5.

For the avoidance of doubt, the phrase 'if necessary or desired' encompasses control of pH to bring it into the defined range as well as control of pH within the defined range. The effective pH of the formulation may be adjusted to the desired value by the addition of alkali, eg. a soluble alkaline salt such as sodium hydroxide or sodium citrate, sodium malate or sodium lactate and by the addition of calcium when present.

The invention also extends to a method of reducing tooth erosion caused by acid in orally administered compositions by orally administering a composition comprising a viscosity modulating polymer material and an acidulant, and optionally containing calcium in the range 0 to 0.8 mol per mol or acid, wherein the effective pH of the

composition is less than or equal to 4.5.

The invention further extends to the use of a composition comprising a viscosity modulating polymer material and an acidulant, optionally containing calcium in the range 0 to 0.8 mol per mol of acid, and having a pH less than or equal to 4.5, in the manufacture of a medicament for the reduction of tooth erosion caused by acid in orally administered compositions.

Oral compositions may contain magnesium or other ions as adjuncts for remineralisation. They may also contain an effective amount of malic acid or potable salts thereof to maintain the solubility of calcium, when present, so as to prevent or minimise the precipitation of insoluble calcium salts. Added malic acid will contribute to the total acidity of the beverage, the remainder of the acidity being provided by other, preferably naturally present, acids such as citric acid, lactic acid and tartaric acid.

Oral compositions may be prepared by mixing the ingredients according to conventional methods. Solid ingredients may be dissolved in aqueous media, eg. water, with heating if required prior to addition to other components. Viscosity modulating polymer materials such as complex polysaccharides are generally hydrated in aqueous media with high shear mixing before addition. Typically beverages and other liquid products are pasteurised prior to filling in bottles or cans or other packs or are "in-pack pasteurised" after filling.

The following examples are illustrative of the invention. Commercial sources for the food grade polymers used in all experiments are as follows:
Xanthan gums sold under trade names Keltrol T, Keltrol RD, Keltrol TF, Keltrol SF, Keltrol BT from Monsanto, Tadworth, Surrey, UK. Xanthan polymer from IFF, Haverhill, Suffolk, UK. Xanthan gum, guar and tragacanth from Thew Arnott & Co. Ltd, Wallington, Surrey, UK. Xanthan gum sold under trade name Satiaxane and xanthan/guar mixture sold under trade name Lygomme MM391 from SKW Biosystems, Newbury, Berkshire, UK. Xanthan/sodium carboxymethylcellulose (35/65%w/w) mixture sold under trade name Grinstead JU543 from Danisco

Ingredients Ltd, Bury St Edmunds, UK. Acacia gum, propylene glycol alginate and sodium carboxymethylcellulose from Red Carnation gums Ltd, Laindon, Essex, UK. Blanose cellulose gum (9M31XF) from Hercules Ltd, Reigate, Surrey, UK. Alginate polymers sold under trade names Kelcoloid LVF, Kelcoloid HVF, Manucol DH and Manucol LF from Monsanto, Tadworth, Surrey, UK. Iota carrageeenan sold under trade name Genuvisco type J and pectins sold under trade names GENU LM 102 AS, GENU LM 104 AS, GENU LM 101 AS, GENU LM 22 CG, GENU LM 12 CG and GENUVIS from Hercules Ltd, Reigate, Surrey, UK. Pectin sold under trade name Unipectin QC40 from SKW Biosytems, Newbury, Berkshire, UK. Polyvinylpyrrolidone sold under the trade name PVP K30 by ISP, NJ, USA.

Example 1

A commercially available ready to drink beverage (pH 3.5) approximating to the following formulation was tested against a control beverage prepared without the addition of xanthan gum.

Ingredients	**Quantity**
Orange juice	110L
Citric Acid	3.8Kg
Acesulfame K	0.74Kg
Aspartame	0.72Kg
Ascorbic Acid	0.29Kg
Orange Flavouring	0.4L
Xanthan Gum (Keltrol T)	0.34Kg
Water to 1000L	

The two beverages were tested for their potential to dissolve enamel in the *in vitro* protocol detailed below in which flat dental enamel sections were exposed to test solutions at a temperature of 37°C for 4 hours. Erosive potential was evaluated by physical measurement of the depth of enamel lost during the procedure. The control beverage without the thickening agent gave an enamel loss of 16 μm over the 4 hour exposure period as compared to the beverage with xanthan gum which gave an

enamel loss of 1 μm.

Protocol for the determination of *in vitro* enamel loss

The erosive potential of the test solutions was determined by measuring the *in vitro* enamel loss over 4 hours in the manner described by Davis & Winter (Davis WB, Winter PJ, British Dental Journal, 1977, 143, 116-119) and West *et al* (West NX *et al*, J Dentistry, 1998, 26(4), 329-335). Recently extracted, caries free, wisdom teeth were sectioned and mounted in epoxy resin blocks with buccal aspect uppermost. The enamel samples were ground, removing a minimum amount of enamel to produce a flat, level block. Baseline measurements were recorded by surfometry and the area to be exposed delineated by the application of PVC tape. 6 masked enamel specimens were exposed to 200mL of test solution for 4 x 1 hour time periods at 37°C with overhead stirring. The test solution was replaced hourly. The enamel samples were subsequently rinsed with deionised water, the PVC tape removed and the tissue loss assessed by surfometry.

Example 2

1000Kg of a powdered orange sports drink was prepared by mixing the following ingredients:

Ingredient	**Quantity (Kg)**
Dextrose monohydrate	400
Maltodextrin	538
Aspartame	0.6
Acesulfame k	0.38
Sodium citrate	17.0
Citric acid	38.0
Ascorbic acid	1.2
Potassium citrate	2.4
Vitamin Premix	0.4
(B2, B6, B12, Niacin, Pantothenic acid)	
Orange flavour	3.0
Beta-Carotene (1%)	6.0
Blanose Cellulose Gum (9M31XF)	1.0

A beverage (pH 3.4) was prepared for consumption by dilution of the powder (50g) in water (500mL).

Example 3

Solutions of citric acid were prepared in deionised water and adjusted to pH 3.8 with 0.1M sodium hydroxide solution. Calcium was added in the form of calcium carbonate and/or xanthan gum was added as Keltrol T. All solutions were tested in a 4 hour *in vitro* protocol as described in Example 1.

Results

Citric Acid Monohydrate (CAMH) (%w/v)	Xanthan Gum (%w/v)	Ca/CAMH Mol Ratio	4hr Enamel Loss (μm)
0.3	0	0	7.6
0.3	0.034	0	5.3
0.3	0	0.3	5.4
0.3	0.034	0.3	2.8

Example 4

Screening of food grade thickening agents for inhibition of dental erosion

Solutions were prepared using a sufficient mass of thickening agent to give a solution of 5-6 cP at 50 rpm (shear rate 61.2 s^{-1}), 37 °C using a Brookfield LVDVII+ viscometer fitted with a UL adaptor. Citric acid buffer was prepared in deionised water using citric acid monohydrate (AR grade, BDH Merck Ltd), preserved with sodium benzoate (0.16g/L, AR grade, BDH Merck Ltd). All Thickening agents were hydrated in buffer by blending for 2 mins using a Silverson high shear mixer, except for guar gum which was stirred overnight at 1000 rpm using a magnetic stirrer. Mixtures of thickening agents were prepared by dry blending prior to hydration. All solutions prepared to give a pH of 3.40 and titratable acidity of 0.3% w/v CAMH. (Citric acid monohydrate). Buffered citric acid (0.3% w/v CAMH, pH 3.40) solution was used as control. Solutions were tested in a 4 hour *in vitro* protocol as described in Example 1.

Thickening Agent	Trade Name (Supplier)	Thickener Conc.(%w/v)	4Hr Enamel Loss (μm)	SD (μm)
Xanthan (clarified)	Keltrol T	0.07	9.8	2.2
Xanthan	(IFF)	0.07	14.7	1.2
Xanthan (clarified dispersible)	Keltrol RD	0.07	6.6	0.8
Xanthan	(Thew Arnott Co.Ltd)	0.07	9.7	1.2
Xanthan (fine mesh)	Keltrol TF	0.07	8.3	0.8
Xanthan	Satiaxane	0.07	14.1	1.6
Xanthan (smooth flow)	Keltrol SF	0.1	7.2	1.3
Xanthan(clarified/salt tolerant)	Keltrol BT	0.07	10.7	2.4
Xanthan/Guar	Lygomme MM391	0.22	14.7	1.7
Xanthan/Sodium carboxymethylcellulose	Grinstead JU543	0.12	13.6	2.1
Acacia gum	(Red Carnation Gums)	10.5	13.7	1.5
Propylene Glycol Alginate (low viscosity)	Kelcoloid LVF	0.59	4.8	0.3
Propylene Glycol Alginate	(Red Carnation Gums)	0.45	6.9	1.8
Propylene Glycol Alginate (high viscosity)	Kelcoloid HVF	0.39	6.3	1.0
Sodium Alginate (medium viscosity)	Manucol DH	0.55	2.6	0.9
Sodium Alginate (low viscosity)	Manucol LF	0.75	2.9	0.5
Guar	(Thew Arnott Co. Ltd)	0.18	11.1	1.2
Tragacanth	(Thew Arnott Co. Ltd)	0.22	11.0	1.8
Iota Carrageenan	Genuvisco type J	0.375	2.7	0.6
High Methoxy Pectin	Unipectin QC40	1	9.9	1.1
Partly Amidated Low Ester Pectin (citrus peel)	GENU LM 102 AS	1	1.6	0.3
Amidated Low Ester Pectin (citrus peel)	GENU LM 104 AS	1	0.7	0.4
Partly Amidated Low Ester Pectin (citrus peel)	GENU LM 101 AS	1.1	2.0	0.8
Low Ester Pectin (citrus peel)	GENU LM 22 CG	1.2	5.7	0.6
Low Ester Pectin (citrus peel)	GENU LM 12 CG	1.1	1.4	0.6
Propylene Glycol Alginate/Low Methoxy Amidated Pectin (50:50)	Kelcoloid LVF & GENU LM 102 AS	0.54	1.53	0.58

Propylene Glycol Alginate /Xanthan (66.6:33.3)	Kelcoloid LVF & Keltrol RD	0.15	7.57	0.45
Control	-	-	24.5	1.9
Control	-	-	20.8	2.0
Control	-	-	24.1	3.8
Control	-	-	30.5	3.17
Control	-	-	19.9	1.53
Control	-	-	29.9	1.53

Example 5

Effect of addition of thickening agent over range of pH and acidity values on inhibition of dental erosion

Solutions were prepared to represent the range of pH and acidity values typically found in a soft drink. Solutions were prepared by shearing the required mass of thickening agent in citric acid buffer, preserved with sodium benzoate (0.16g/L), for 2 minutes using a Silverson high shear mixer. The pH was adjusted to the required value by the addition of 1M NaOH. All solutions gave viscosity values of 5 to 6 cP (Brookfield LVDVII + UL adaptor, 50 rpm, 37°C). Solutions were tested in a 4 hour *in vitro* protocol as described in Example 1. The results demonstrate the efficacy of the technology in reducing enamel loss over a range of pH values and viscosities.

Thickening Agent	Th.Conc. (%w/v)	pH	Acidity (%w/w CAMH)	4 Hr Enamel Loss (μm)	SD (μm)
Control	-	2.5	0.1	63.4	4.4
Keltrol RD	0.07	2.5	0.1	8.7	1.2
Keltrol RD	0.07	2.5	0.3	9.7	1.2
Kelcoloid LVF	0.59	2.5	0.3	11.5	3.6
Control	-	2.5	0.3	41.04	0.2
Control	-	2.5	0.3	30.4	6.1
Keltrol RD	0.07	3.0	0.7	13.5	1.6
Control	-	3.0	0.7	34.2	3.8
Kelcoloid LVF	0.55	3.0	0.3	11.6	3.0
Keltrol RD	0.07	3.0	0.3	7.84	1.1

Control	-	3.0	0.3	23.2	0.4
Control	-	3.0	0.3	26.3	2.5
Keltrol RD	0.07	4.5	1.0	7.1	1.3
Kelcoloid LVF	0.59	4.5	1.0	11.4	1.0
Control	-	4.5	1.0	21.2	1.8

Example 6

Determination of the effect of viscosity and type of thickening agent on *in vitro* enamel loss

Viscosity versus concentration plots were determined for two commercially available food gums, a high ester citrus pectin (GENUVIS) and finely milled xanthan gum (Keltrol T). Gums were hydrated in a 0.3% w/v citric acid monohydrate buffer, adjusted to pH 3.4 with 1M NaOH. A controlled strain Rheometrix RFSII viscometer (with cuette geometry) was run at 37°C and concentration v viscosity plots produced using a shear rate of 125 s^{-1}. Concentrations of the two gums were determined to give viscosity values of 2.5cP, 5.0cP, 10cP and 20cP under the conditions used. A viscosity v concentration profile for a sodium carboxymethyl cellulose gum (Red Carnation gums Ltd) was determined using a Brookfield LVDVII+ viscometer (fitted with a UL adaptor at 60 rpm (104 s^{-1}) at 37°C). The approximate concentration required to give a viscosity of 20cP under these conditions was estimated by extrapolation from the plot. Solutions were tested for *in vitro* enamel loss using the screening protocol described in Example 1.

Results

Viscosity (cP)	%w/v xanthan	% w/v pectin	%w/v CMC	4Hr Enamel loss - xanthan (μm)	4Hr Enamel loss - pectin (μm)	4Hr Enamel loss - CMC (μm)
2.5	0.05	0.67	-	8.7	11.5	-
5	0.08	0.9	0.17	7.8	12.0	31.0
10	0.14	1.20	-	2.3	9.0	-
20	0.24	1.6	0.39	2.5	2.7	13.5

Low-methoxy amidated pectin (GENU LM 102 AS) and low viscosity propylene glycol alginate (Kelcoloid LVF) were tested in the model of erosive potential at different concentrations. Each solution of gum was hydrated using a 0.3% w/v citric acid monohydrate buffer at pH 3.40. Viscosities were determined using a Brookfield LVDVII+ viscometer (fitted with a UL adaptor) at 50 rpm (shear rate 61.2s^{-1}) and 37°C.

GENU LM 102 AS (%w/v)	Viscosity (cP)	4Hr Enamel Loss (μm)
1.0	5.7	1.6
0.75	3.8	3.4
0.5	2.3	1.0

Kelcoloid LVF (%w/v)	Viscosity (cP)	4Hr Enamel Loss (μm)
0.59	6.7	4.8
0.45	3.5	6.7

The results confirm that viscosity is not the primary factor influencing erosive potential in this model. A general decrease in enamel loss was found with increasing viscosity for each material tested but enamel losses were not equivalent, suggesting that erosive potential is product type specific, particularly at viscosity values of 10cP or less which are most suitable for the formulation of acidic compositions with low erosive potential.

Example 7

Effect of thickening agent and calcium on dental erosion

Test formulations of typical pH and acidity for a ready to drink fruit beverage were prepared using stock solutions of citric acid buffer (300g/L) and sodium benzoate preservative (16g/L). Solutions were blended for 2 minutes using a Silverson high shear mixer. Viscosities were determined using a Brookfield LVDVII+ viscometer (fitted with a UL adaptor) at 50 rpm (shear rate 61.2s^{-1}) and 37°C. Solutions were tested for *in vitro* enamel loss using the screening protocol described in Example 1. The results show that addition of a thickening agent and calcium to acid

compositions confers low erosive potential at calcium levels and pH values below those which are required in the absence of a thickening agent.

Ingredient	Test Solution A	Test Solution B
Deionised water	800 ml	800 ml
Benzoate stock solution	20 ml	20 ml
Xanthan gum (Keltrol RD)	1.8 g	2.0 g
Citric Acid stock solution	20 ml	20 ml
Calcium carbonate	0.28 g	0.157 g
Deionised water	to 1800 ml	to 1800 ml
1M NaOH	to pH 3.40	to pH 3.20
Deionised water	to 2 L (volumetric)	to 2 L (volumetric)

Test Solution	Viscosity (cP)	pH	Titratable Acidity (%w/w CAMH)	Ca/Acid Ratio	4 Hr Enamel Loss (μm)
A	8	3.4	0.3	0.1	1.4
B	9	3.2	0.3	0.05	3.3

Example 8

Ready to Drink Blackcurrant Juice Beverages

A base syrup was prepared as follows:

Sodium benzoate (0.80g) was dissolved in warm treated water and diluted to approximately 200ml with treated water. Blackcurrant concentrate (88.2ml) was added followed by solutions of ascorbic acid (2.55g) and aspartame (1.60g), acesulfame K (0.50g), and potassium sorbate (1.52g), in treated water. Blackcurrant flavour (1.14ml) was added to the mixing batch and the volume was corrected to 1 litre with treated water.

Two ready to drink beverage formulations were prepared as follows:

Thickening agent was added to water (2.5 litres) with stirring using a high shear Silverson mixer and mixing continued to form a solution. Calcium carbonate (where present) was dissolved in treated water and slowly added to the solution. Base syrup (1 litre) was added with mixing to form a homogenous solution and volume was adjusted to 5 litres with water. The pH was corrected to 3.4 with 1M sodium

hydroxide. Viscosity was measured using a Brookfield LVDII+ viscometer with UL adaptor at 50 rpm and 37 C. Titratable acidity for both formulations (%w/w CAMH) was 0.4. The formulations were tested for *in vitro* enamel loss using the screening protocol described in Example 1.

Thickening Agent (g)	$CaCO_3$ (g)	Ca/Acid molar ratio	Viscosity (cP)	4Hr Enamel Loss (μm)
Kelcoloid LVF (29.5)	-	-	6.7	3.6
Keltrol RD (4.5)	0.7	0.1	7.6	6.2

Example 9

Ready to Drink Sparkling Raspberry Flavoured Beverage

Pectin thickener (GENU LM 102 AS) (37.5g) was sprinkled into warm water (1 litre) with high shear mixing using a Silverson mixer. Solutions of potassium sorbate (1.28g), acesulfame K (0.27g), citric acid (14.0g) and aspartame (1.20g) and ascorbic acid (1.50g) and potassium citrate (4.81g) were prepared separately and added to the pectin batch with mixing. Raspberry flavouring (2.51ml), and cochineal red colour (0.50ml) dispersed in water were added to the mix forming a base syrup which was diluted with water to 1.67 litres. The base syrup was diluted (1 part syrup to 2 parts water) with carbonated water to form a sparkling drink. Viscosity was measured using a Brookfield LVDII+ viscometer with UL adaptor at 50rpm and 37 C. The product was tested for *in vitro* enamel loss using the screening protocol described in Example 1.

The product had the following parameters:

pH	:	3.5
Acidity (%w/w CAMH)	:	0.4
Viscosity (cP)	:	3.2
Enamel loss (m)	:	3.67

Example 10

Ready to Drink Cola Flavoured Sparkling Beverage

A cola concentrate was made by mixing the following ingredients:

Phosphoric acide 85%	:	1 litre
Caffeine BP	:	130g

Cola emulsion	:	0.75 litre
Caramel double strength	:	3.125 litre
Water to	:	10 litre

A cola syrup was made by mixing the following ingredients:

Sugar syrup 67 Brix	:	70 litre
(or aspartame	:	300g)
Cola concentrate	:	2.5 litre
Cola flavour booster	:	0.06 litre
Xanthan (Keltrol RD)	:	420g
Water to	:	100 litre

The cola syrup was diluted (1 part syrup to 5 parts water) with carbonated water to form a sparkling drink with a pH of approximately 2.5.

Example 11

Effect of Polyvinyl pyrrolidone on Inhibition of Dental Erosion

Citric acid buffer (0.3%w/v citric acid monohydrate) was prepared in deionised water with the addition of sodium benzoate (0.16g/L) as a preservative. The solution was adjusted to pH 3.4 with 1M NaOH. Polyvinylpyrolidone (PVP-K30, 125 g/L) was added to the solution with stirring and the resulting solution stirred for 20 minutes. This gave a solution of pH 3.4, titratable acidity 0.3% w/w CAMH, viscosity 4.7 cP (37°C, 50rpm, Brookfield LVDVII+, UL adaptor). The solution was gave an enamel loss of 13.8 μm as compared to an enamel loss of 25 μm from a control buffer solution when tested over 4 hours in the *in vitro* erosivity screening protocol

Example 12

Mouthwash Formulation

A mouthwash was prepared using from following ingredients:

Ingredient	**%w/w**
Ethanol 96% BP	8
Soluble saccharin	0.06

Cetylpyridinium chloride	0.05
Tego Betain CK-KB5	0.2
Flavouring	0.12
Sodium acetate trihydrate	0.05
Acetic acid 80%	0.1575
PVP-K30	12.5
Calcium chloride dihydrate	0.123
Deionised water	78.74

The ethanol, cetylpyridinium chloride, Tego Betain CK-KB5 (trade name for a cocamido propyl betaine) and flavouring were mixed together to form a clear solution. In a separate container, the remainder of the ingredients were mixed together and stirred for 20 minutes. The ethanolic solution was then added to the aqueous solution to produce a mouthwash with a pH of 4.5 and a calcium to acid molar ratio of 0.4.

CLAIMS

1. Use of a viscosity modulating polymer material as a tooth erosion inhibitor in an acidic composition for oral administration wherein the effective pH of the composition is less than or equal to 4.5.

2. Use as claimed in claim 1 wherein the viscosity modulating polymer is a complex polysaccharide material.

3. Use as claimed in claim 2 wherein the complex polysaccharide material is an alginate, a xanthan or a pectin.

4. Use as claimed in any one of claims 1 to 3 wherein the effective pH of the composition is from 2.0 to 4.5.

5. Use as claimed in any one of claims 1 to 4 wherein the acidulant comprises citric acid, malic acid, lactic acid, tartaric acid, phosphoric acid, acetic acid or mixtures thereof.

6. Use as claimed in any one of claims 1 to 5 wherein the acidic composition contains a calcium compound such that calcium is present in the composition in an amount up to 0.8 mol per mol of acid.

7. Use as claimed in claim 6 wherein the calcium source is a soluble calcium salt.

8. Use as claimed in any one of claims 1 to 7 wherein the acidic composition is a beverage or a liquid or solid concentrate for the preparation of a beverage.

9. Use as claimed in claim 8 wherein the beverage is a health drink.

10. Use as claimed in any one of claims 1 to 7 wherein the acidic composition is an oral healthcare product.

11. Use as claimed in claim 8 wherein the beverage has a pH in the range 2.5 to 4.0.

12. Use as claimed in claim 8 wherein the beverage has a titratable acidity in the range 0.01 to 4%w/w.

13. A method of reducing the tooth erosion potential of an acidic composition for oral use comprising adding a viscosity modulating polymer material, and optionally calcium in the range 0 to 0.8 mol per mol of acid, to an acidic oral composition and, if necessary or desired, controlling the effective pH so that it is less than or equal to 4.5.

14. A method of reducing tooth erosion caused by acid in orally administered compositions by orally administering a composition comprising a viscosity modulating polymer material and an acidulant, and optionally containing calcium in the range 0 to 0.8 mol per mol or acid, wherein the effective pH of the composition is less than or equal to 4.5.

15. The use of a composition comprising a viscosity modulating polymer material and an acidulant, optionally containing calcium in the range 0 to 0.8 mol per mol of acid, and having a pH less than or equal to 4.5, in the manufacture of a medicament for the reduction of tooth erosion caused by acid in orally administered compositions.

16. A composition for oral use comprising an acidulant, a viscosity modulating polymer material and a calcium compound wherein calcium is present in the composition in an amount up to 0.8 mol per mol of acid and the effective pH of the composition is less than or equal to 4.5.

INTERNATIONAL SEARCH REPORT

In: ational Application No
PCT/EP 99/06423

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A23L1/05 A23L2/52 A61K7/00 A61K7/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A23L A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	W.A.VAN DER REIJDEN ET AL.: "Influence of Polymers for Use in Saliva Substitutes on DE- and Remineralization of Enamel in vitro" CARIES RESEARCH, vol. 31, no. 3, - June 1997 (1997-06) pages 216-223, XP002128236 basel cited in the application the whole document ---	1-16
A	FR 2 731 588 A (SYSTEMES BIO INDUSTRIES) 20 September 1996 (1996-09-20) page 4, line 26 -page 5, line 10; claims; examples 1-3 --- -/--	1-5,8,9, 11,12

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
20 January 2000	20. 03. 2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Van Moer, A

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	PATENT ABSTRACTS OF JAPAN vol. 017, no. 513 (C-1111), 16 September 1993 (1993-09-16) & JP 05 139979 A (LOTTE CO LTD), 8 June 1993 (1993-06-08) abstract	1-16
A	PATENT ABSTRACTS OF JAPAN vol. 012, no. 191 (C-501), 3 June 1988 (1988-06-03) & JP 62 294607 A (KANEBO LTD;OTHERS: 01), 22 December 1987 (1987-12-22) abstract	1-16
A	EP 0 719 783 A (EZAKI GLICO) 3 July 1996 (1996-07-03) page 2, line 11-16 page 3, line 30-43 page 4, line 35-38; claims	1-16

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 99/06423

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 13,14 and 15 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos..
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Ir. ational Application No
PCT/EP 99/06423

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		US 5861048 A	19-01-1999